Chapter 728

Assurance for Superiority by a Margin Tests for the Difference of Two Hazard Rates Assuming an Exponential Model

Introduction

This module calculates the assurance of *superiority by a margin* tests for the difference of two hazard rates which assume an exponential model. These results can also be used for a logrank test and a proportional hazards test. The assurance calculation in this procedure is based on a user-specified prior distribution of the applicable parameters. This procedure may also be used to determine the needed sample size to obtain a specified assurance.

The procedure is based on the *unconditional* method of Chow, Shao, and Wang (2008) which, in turn, is based on the *conditional* methods of Lachin and Foulkes (1986). The conditional procedure does not extend to superiority, non-zero null, or equivalence tests as easily as the unconditional method does (see Chow, Shao, and Wang (2008) page 173). The power calculations are based on the **PASS** procedure *Superiority by a Margin Tests for the Difference of Two Hazard Rates Assuming an Exponential Model.* Refer to that procedure for more details on the test.

The assurance calculation used in this procedure is based on O'Hagan, Stevens, and Campbell (2005).

Assurance

The assurance of a design is the expected value of the power with respect to one or more prior distributions of the design parameters. Assurance is also referred to as *Bayesian assurance*, *expected power*, *average power*, *statistical assurance*, *hybrid classical-Bayesian procedure,* or *probability of success*.

The power of a design is the probability of rejecting the null hypothesis, conditional on a given set of design attributes, such as the test statistic, the significance level, the sample size, and the effect size to be detected. As many of the parameters are typically unknown quantities, the stated power may be very different from the true power if the specified parameter values are inaccurate.

While power is conditional on individual design parameter values, and is highly sensitive to those values, assurance is the average power across a presumed prior distribution of the parameters. Thus, assurance adds a Bayesian element to the frequentist framework, resulting in a hybrid approach to the probability of trial or study success. It should be noted that when it comes time to perform the statistical test on the resulting data, these methods for calculating assurance assume that the traditional (frequentist) tests will be used.

The next section describes some of the ways in which the prior distributions for effect size parameters may be determined.

Elicitation

In order to calculate assurance, a suitable prior distribution for the applicable parameters must be determined. This process is called the *elicitation* of the prior distribution.

The elicitation may be as simple as choosing a distribution that seems plausible for the parameter(s) of interest, or as complex as combining the informed advice of several experts based on experience in the field, available pilot data, or previous studies. The accuracy of the assurance value depends on the accuracy of the elicited prior distribution. The assumption (or hope) is that an informed prior distribution will produce a more accurate estimate of the probability of trial success than a single value estimate. Because clinical trials and other studies are often costly, many institutions now routinely require an elicitation step.

Two reference texts that focus on elicitation are O'Hagan, Buck, Daneshkhah, Eiser, Garthwaite, Jenkinson, Oakley, and Rakow (2006) and Dias, Morton, and Quigley (2018).

Technical Details

We assume that a study is to be made to compare the hazard rates of a control group and an experimental group using a superiority by a margin test. The control group (group 1) consists of patients that will receive the existing treatment. In cases where no existing treatment exists, group 1 consists of patients that will receive a placebo. Group 2 will receive the new treatment.

We assume that the critical event of interest is death and that two treatments have survival distributions with instantaneous death (hazard) rates, λ_1 and λ_2. These hazard rates are a subject's probability of death in a short period of time. The survival times are assumed to be exponential. This section presents the *unconditional* method of Chow, Shao, and Wang (2008).

Basic Model

Suppose a clinical trial consists of two independent groups labeled "1" and "2" (where group 1 is the control group and group 2 is the treatment group). The total sample size is N and the sizes of the two groups are N_1 and N_2. Usually, you would plan to have $N_1 = N_2$.

Clinical Superiority Hypothesis

Assuming that <u>lower hazard rates are better</u>, clinical superiority is established by concluding that the treatment hazard rate is lower than the control hazard rate by at least a small margin Δ. The statistical hypotheses that yields this conclusion when the null hypothesis is rejected is

$$H_0: (\lambda_2 - \lambda_1) \geq -\Delta \quad \text{versus} \quad H_1: (\lambda_2 - \lambda_1) < -\Delta$$

or

$$H_0: \lambda_2 \geq \lambda_1 - \Delta \quad \text{versus} \quad H_1: \lambda_2 < \lambda_1 - \Delta$$

If, however, higher hazard rates are better, superiority by a margin is established by concluding that the treatment hazard rate is at most, only slightly lower than the control hazard rate. The statistical hypotheses that yields this conclusion when the null hypothesis is rejected is

$$H_0: (\lambda_2 - \lambda_1) \le \Delta \quad \text{versus} \quad H_1: (\lambda_2 - \lambda_1) > \Delta$$

or

$$H_0: \lambda_2 \le \lambda_1 + \Delta \quad \text{versus} \quad H_1: \lambda_2 > \lambda_1 + \Delta$$

Test Statistic

The power and sample size formulas presented below are for the difference of two exponential hazard rates. Simulation studies have shown that they also approximate the power of the logrank test. It is anticipated that the actual test statistic is the regression coefficient from a Cox regression.

Test Comparing Hazard Rates

The original test statistic is the difference of the hazard rates estimated by maximum likelihood divided by their standard error. The maximum likelihood estimate of an exponential hazard rate for a particular group is

$$\hat{\lambda} = \frac{\text{number of events}}{\text{sum of study time of all subjects}}$$

Chow, Shao, and Wang (2008) indicate that the test statistic

$$Z = \frac{(\hat{\lambda}_2 - \hat{\lambda}_1) - \Delta}{\sqrt{\dfrac{\sigma^2(\hat{\lambda}_1)}{N_1} + \dfrac{\sigma^2(\hat{\lambda}_2)}{N_2}}}$$

where

$$\sigma^2(\lambda) = \frac{\lambda^2}{1 + \dfrac{e^{-\lambda T}(1 - e^{\lambda R})}{\lambda R}}$$

follows the standard normal standard normal distribution at least approximately.

Power Calculations

Assuming an exponential model with hazard rates λ_1 and λ_2 for the two groups, Chow et al. (2008) give the following equation relating N and power of a two-tailed test.

$$\frac{(\lambda_2 - \lambda_1) + \Delta}{\sqrt{\dfrac{\sigma^2(\lambda_1, \omega_1, G)}{N_1} + \dfrac{\sigma^2(\lambda_2, \omega_2, G)}{N_2}}} - z_{1-\alpha/2} = z_{1-\beta}$$

where

$$\sigma^2(\lambda_i, \omega_i, G) = \frac{\lambda_i^2}{E(d_i | \lambda_i, \omega_i, G)}$$

$$E(d_i | \lambda_i, \omega_i, G) = \left(\frac{\lambda_i}{\lambda_i + \omega_i}\right)\left(1 + \frac{G \exp\{-(\lambda_i + \omega_i)T\}[1 - \exp\{(\lambda_i + \omega_i - G)R\}]}{(\lambda_i + \omega_i - G)[1 - \exp\{-GR\}]}\right)$$

$$E(d_i | \lambda_i, \omega_i, 0) = \left(\frac{\lambda_i}{\lambda_i + \omega_i}\right)\left(1 + \frac{\exp\{-(\lambda_i + \omega_i)T\}[1 - \exp\{(\lambda_i + \omega_i)R\}]}{(\lambda_i + \omega_i)R}\right)$$

These parameters are interpreted as follows:

Parameter	Interpretation
$\sigma^2(\lambda, \omega, G)$	Variance of $\hat{\lambda}$
$E(d_i | \lambda_i, \omega_i, G)$	Expected proportion of events (deaths) in group i
d_i	Indicates a person does ($d_i = 1$) or does not ($d_i = 0$) die in group i
λ_i	Hazard rate of group i (see below)
ω_i	Loss to follow-up hazard rate of group i (see below)
A	Patient entry parameter (see below)
R	Accrual time
T	Total time
$T - R$	Follow-up time

Exponential Distribution

The hazard rate from the exponential distribution, λ, is usually estimated using maximum likelihood techniques. In the planning stages, you have to obtain an estimate of this parameter. To see how to accomplish this, let's briefly review the exponential distribution. The density function of the exponential is defined as

$$f(t) \;=\; \lambda \exp\{-\lambda t\}, \;\; t \geq 0, \lambda > 0.$$

The cumulative survival distribution function is

$$S(t) \;=\; \exp\{-\lambda t\}, \;\; t \geq 0.$$

Solving this for λ yields

$$\lambda \;=\; -\frac{\log\{S(t)\}}{t}$$

Note that $S(t)$ gives the probability of surviving t years. To obtain a planning estimate of λ, you need only know the proportion surviving during a particular time period. You can then use the above equation to calculate λ.

Patient Entry

Patients are enrolled during the accrual period. **PASS** lets you specify the pattern in which subjects are enrolled. Suppose patient entry times are distributed as $g(t)$ where t_i is the entry time of the ith individual and $0 \leq t_i \leq R$. Let $g(t)$ follow the truncated exponential distribution with parameter G, which has the density

$$g(t) \;=\; \begin{cases} \dfrac{G \exp\{-Gt\}}{1 - G \exp\{-GR\}} & \text{if } 0 \leq t \leq R, \;\; G \neq 0 \\[2em] 1 & \text{otherwise} \end{cases}$$

where

> R is accrual time.

> G is interpreted as follows:

> $G > 0$ results in a convex (faster than expected) entry distribution.

> $G < 0$ results in a concave (slower than expected) entry distribution.

> $G = 0$ results in the uniform entry distribution in which $g(t) = 1/R$.

Rather than specify G directly, **PASS** has you enter the percentage of the accrual time (called A) that will be needed to enroll 50% of the subjects. Using an iterative search, the value of G corresponding to this percentage is calculated and used in the calculations.

Losses to Follow-Up

The staggered patient entry over the accrual period results in censoring times ranging from *T* - *R* to *T* years during the follow-up period. This is often referred to as administrative censoring, since it is caused by the conclusion of the study rather than by some random factor working on an individual. To model the losses to follow-up in each group which come from other causes, we use the exponential distribution again, this time with hazard rates ω_1 and ω_2. You can obtain appropriate loss-to-follow-up hazard rates using the following formula or by using the Survival Parameter Conversion Tool available from the Tools menu or by pressing the small button to the rate of the loss-to-follow-up hazard rate box.

$$\omega = -\frac{\log\{1 - P_{loss}(R)\}}{R}$$

Assurance Calculation

This assurance computation described here is based on O'Hagan, Stevens, and Campbell (2005).

Let $P_1(H|\lambda_1, \lambda_2, \omega_1, \omega_2, A)$ be the power function described above where *H* is the event that the null hypothesis is rejected conditional on a specific set of parameter values. The specification of $\lambda_1, \lambda_2, \omega_1, \omega_2,$ and A is critical to the power calculation, but the actual values are seldom known. Assurance is defined as the expected power where the expectation is with respect to a joint prior distribution for $\lambda_1, \lambda_2, \omega_1, \omega_2,$ and A. Hence, assurance is

$$Assurance = E_{\lambda_1, \lambda_2, \omega_1, \omega_2, A}\big(P_1(H|\lambda_1, \lambda_2, \omega_1, \omega_2, A)\big)$$

$$= \int \int \int \int \int P_1(H|\lambda_1, \lambda_2, \omega_1, \omega_2, A) f(\lambda_1, \lambda_2, \omega_1, \omega_2, A) d\lambda_1 d\lambda_2 d\omega_1 d\omega_2 dA$$

where $f(\lambda_1, \lambda_2, \omega_1, \omega_2, A)$ is the joint prior density of $\lambda_1, \lambda_2, \omega_1, \omega_2,$ and A.

In **PASS**, the joint prior distribution can be specified as either a discrete approximation to the joint prior distribution, or as individual prior distributions, one for each parameter.

Specifying a Joint Prior Distribution

If the joint prior distribution is to be specified directly, the distribution is specified in **PASS** using a discrete approximation to the function $f(\lambda_1, \lambda_2, \omega_1, \omega_2, A)$. This provides flexibility in specifying the joint prior distribution. In the five-parameter case, six columns are entered on the spreadsheet: five for the parameters and a sixth for the probability. Each row gives a value for each parameter and the corresponding parameter-combination probability. The accuracy of the distribution approximation is controlled by the number of points (spreadsheet rows) that are used.

An example of entering a joint prior distribution is included at the end of the chapter.

Specifying Individual Prior Distributions

Ciarleglio, Arendt, and Peduzzi (2016) suggest that more flexibility is available if the joint prior distribution is separated into five independent univariate distributions as follows:

$$f(\lambda_1, \lambda_2, \omega_1, \omega_2, A) = f_1(\lambda_1)f_2(\lambda_2)f_3(\omega_1)f_4(\omega_2)f_5(A)$$

where $f_1(\lambda_1)$ is the prior distribution of λ_1, $f_2(\lambda_2)$ is the prior distribution of λ_2, and so on. This is the definition that is used in **PASS**. The definition of assurance becomes

$$Assurance = E_{\lambda_1, \lambda_2, \omega_1, \omega_2, A}\big(P_1(H|\lambda_1, \lambda_2, \omega_1, \omega_2, A)\big)$$

$$= \int \int \int \int \int P_1(H|\lambda_1, \lambda_2, \omega_1, \omega_2, A)f_1(\lambda_1)f_2(\lambda_2)f_3(\omega_1)f_4(\omega_2)f_5(A)d\lambda_1 d\lambda_2 d\omega_1 d\omega_2 dA$$

Using this definition, the assurance can be calculated using numerical integration. There are a variety of pre-programmed, univariate prior distributions available in **PASS**.

Fixed Values (No Prior) and Custom Values

For any given parameter, **PASS** also provides the option of entering a single fixed value for the prior distribution, or a series of values and corresponding probabilities (using the spreadsheet), rather than one of the pre-programmed distributions.

Numerical Integration in PASS (and Notes on Computation Speed)

When the prior distribution is specified as independent univariate distributions, **PASS** uses a numerical integration algorithm to compute the assurance value as follows:

The domain of each prior distribution is divided into M intervals. Since many of the available prior distributions are unbounded on one (e.g., Gamma) or both (e.g., Normal) ends, an approximation is made to make the domain finite. This is accomplished by truncating the distribution to a domain between the two quantiles: $q_{0.001}$ and $q_{0.999}$.

The value of M controls the accuracy and speed of the algorithm. If only one parameter is to be given a prior distribution, then a value of M between 50 and 100 usually gives an accurate result in a timely manner. However, if two parameters are given priors, the number of iterations needed increases from M to M^2. For example, if M is 100, 10000 iterations are needed. Reducing M from 100 to 50 reduces the number of iterations from 10000 to 2500.

The algorithm runtime increases when searching for sample size rather than solving for assurance, as a search algorithm is employed in this case. When solving for sample size, we recommend reducing M to 20 or less while exploring various scenarios, and then increasing M to 50 or more for a final, more accurate, result.

List of Available Univariate Prior Distributions

This section lists the univariate prior distributions that may be used for any of the applicable parameters when the Prior Entry Method is set to Individual.

No Prior

If 'No Prior' is chosen for a parameter, the parameter is assumed to take on a single, fixed value with probability one.

Beta (Shape 1, Shape 2, a, c)

A random variable X that follows the beta distribution is defined on a finite interval [a, c]. Two shape parameters (α and β) control the shape of this distribution. Two location parameters a and c give the minimum and maximum of X.

The probability density function of the beta distribution is

$$f(x|\alpha,\beta,a,c) = \frac{\left(\frac{x-a}{c-a}\right)^{\alpha-1}\left(\frac{c-x}{c-a}\right)^{\beta-1}}{(c-a)B(\alpha,\beta)}$$

where $B(\alpha,\beta) = \Gamma(\alpha)\,\Gamma(\beta)/\,\Gamma(\alpha+\beta)$ and $\Gamma(z)$ is the gamma function.

The mean of X is

$$\mu_X = \frac{\alpha c + \beta a}{\alpha + \beta}$$

Various distribution shapes are controlled by the values of α and β. These include

Symmetric and Unimodal

   $\alpha = \beta > 1$

U Shaped

   $\alpha = \beta < 1$

Bimodal

   $\alpha, \beta < 1$

Uniform

   $\alpha = \beta = 1$

Parabolic

$$\alpha = \beta = 2$$

Bell-Shaped

$$\alpha = \beta > 2$$

Gamma (Shape, Scale)

A random variable X that follows the gamma distribution is defined on the interval $(0, \infty)$. A shape parameter, κ, and a scale parameter, θ, control the distribution.

The probability density function of the gamma distribution is

$$f(x|\kappa, \theta) = \frac{x^{\kappa-1}e^{-\frac{x}{\theta}}}{\theta^{\kappa}\Gamma(\kappa)}$$

where $\Gamma(z)$ is the gamma function.

The mean of X is

$$\mu_X = \frac{\kappa}{\theta}$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where Min and Max are two truncation bounds.

Inverse-Gamma (Shape, Scale)

A random variable X that follows the inverse-gamma distribution is defined on the interval $(0, \infty)$. If $Y \sim$ gamma, then $X = 1 / Y \sim$ inverse-gamma. A shape parameter, α, and a scale parameter, β, control the distribution.

The probability density function of the inverse-gamma distribution is

$$f(x|\alpha, \beta) = \frac{\beta^{\alpha}x^{-\alpha-1}e^{-\frac{\beta}{x}}}{\Gamma(\alpha)}$$

where $\Gamma(z)$ is the gamma function.

The mean of X is

$$\mu_X = \frac{\beta}{\alpha - 1} \text{ for } \alpha > 1$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where Min and Max are two truncation bounds.

Logistic (Location, Scale)

A random variable X that follows the logistic distribution is defined on the interval $(-\infty, \infty)$. A location parameter, μ, and a scale parameter, s, control the distribution.

The probability density function of the logistic distribution is

$$f(x|\mu, s) = \frac{e^{-\frac{x-\mu}{s}}}{s\left(1 + e^{-\frac{x-\mu}{s}}\right)^2}$$

The mean of X is

$$\mu_X = \mu$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

Lognormal (Mean, SD)

A random variable X that follows the lognormal distribution is defined on the interval $(0, \infty)$. A location parameter, $\mu_{\log(X)}$, and a scale parameter, $\sigma_{\log(X)}$, control the distribution. If Z ~ standard normal, then $X = e^{\mu+\sigma Z} \sim$ lognormal. Note that $\mu_{\log(X)} = E(\log(X))$ and $\sigma_{\log(X)} = Standard\ Deviation(\log(X))$.

The probability density function of the lognormal distribution is

$$f(x|\mu, \sigma) = \frac{e^{-\frac{1}{2}\left(\frac{\log x - \mu}{\sigma}\right)^2}}{x\sigma\sqrt{2\pi}}$$

The mean of X is

$$\mu_X = e^{\mu+\frac{\sigma^2}{2}}$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

LogT (Mean, SD)

A random variable X that follows the logT distribution is defined on the interval $(0, \infty)$. A location parameter, $\mu_{\log(X)}$, a scale parameter, $\sigma_{\log(X)}$, and a shape parameter, ν, control the distribution. Note that ν is referred to as the *degrees of freedom*.

If t ~ Student's t, then $X = e^{\mu + \sigma t} \sim$ logT.

The probability density function of the logT distribution is

$$f(x|\mu, \sigma, \nu) = \frac{\Gamma\left(\frac{\nu+1}{2}\right)}{x\Gamma\left(\frac{\nu}{2}\right)\sigma\sqrt{\nu\pi}}\left(1 + \frac{1}{\nu}\left(\frac{\log x - \mu}{\sigma}\right)^2\right)^{\left(\frac{-\nu-1}{2}\right)}$$

The mean of X is not defined.

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

Normal (Mean, SD)

A random variable X that follows the normal distribution is defined on the interval $(-\infty, \infty)$. A location parameter, μ, and a scale parameter, σ, control the distribution.

The probability density function of the normal distribution is

$$f(x|\mu, \sigma) = \frac{e^{-\frac{1}{2}\left(\frac{x-\mu}{\sigma}\right)^2}}{\sigma\sqrt{2\pi}}$$

The mean of X is

$$\mu_X = \mu$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

T (Mean, SD, DF)

A random variable X that follows Student's t distribution is defined on the interval $(-\infty, \infty)$. A location parameter, μ, a scale parameter, σ, and a shape parameter, ν, control the distribution. Note that ν is referred to as the *degrees of freedom* or *DF*.

The probability density function of the Student's t distribution is

$$f(x|\mu, \sigma, \nu) = \frac{\Gamma\left(\frac{\nu+1}{2}\right)}{\Gamma\left(\frac{\nu}{2}\right)\sigma\sqrt{\nu\pi}}\left(1 + \frac{1}{\nu}\left(\frac{x - \mu}{\sigma}\right)^2\right)^{\left(\frac{-\nu-1}{2}\right)}$$

The mean of X is μ if $\nu > 1$.

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

Triangle (Mode, Min, Max)

Let a = minimum, b = maximum, and c = mode. A random variable X that follows a triangle distribution is defined on the interval (a, b).

The probability density function of the triangle distribution is

$$f(x|a, b, c) = \begin{cases} \dfrac{2(x-a)}{(b-a)(c-a)} & \text{for } a \leq x < c \\[2mm] \dfrac{2}{b-a} & \text{for } x = c \\[2mm] \dfrac{2(b-x)}{(b-a)(b-c)} & \text{for } c < x \leq b \end{cases}$$

The mean of X is

$$\frac{a+b+c}{3}$$

Uniform (Min, Max)

Let a = minimum and b = maximum. A random variable X that follows a uniform distribution is defined on the interval $[a, b]$.

The probability density function of the uniform distribution is

$$f(x|a, b) = \begin{cases} \dfrac{1}{b-a} & \text{for } a \leq x \leq b \end{cases}$$

The mean of X is

$$\frac{a+b}{2}$$

Weibull (Shape, Scale)

A random variable X that follows the Weibull distribution is defined on the interval $(0, \infty)$. A shape parameter, κ, and a scale parameter, λ, control the distribution.

The probability density function of the Weibull distribution is

$$f(x|\kappa, \lambda) = \frac{\kappa}{\lambda} \left(\frac{x}{\lambda}\right)^{\kappa-1} e^{-\left(\frac{x}{\lambda}\right)^{\kappa}}$$

The mean of X is

$$\mu_X = \kappa\Gamma\left(1 + \frac{1}{\kappa}\right)$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where Min and Max are two truncation bounds.

Custom (Values and Probabilities in Spreadsheet)

This custom prior distribution is represented by a set of user-specified points and associated probabilities, entered in two columns of the spreadsheet. The points make up the entire set of values that are used for this parameter in the calculation of assurance. The associated probabilities should sum to one. Note that custom values and probabilities can be used to approximate any continuous distribution.

For example, a prior distribution of X might be

X_i	P_i
10	0.2
20	0.2
30	0.3
40	0.2
50	0.1

In this example, the mean of X is

$$\mu_X = \sum_{i=1}^{5} X_i P_i$$

Example 1 – Assurance Over a Range of Sample Sizes

A researcher is planning a clinical trial using a parallel, two-group, equal sample allocation design to compare the survivability of a new treatment with that of the current treatment using a one-sided, superiority by a margin test with a significance level of 0.025. The hazard rates of the control and treatment groups are expected to be 0.7 and 0.45, respectively.

The trial will include a recruitment period of one-year after which participants will be followed for an additional two-years. It is assumed that patients will enter the study uniformly over the accrual period. The researcher estimates a loss-to-follow hazard rate of 0.1 in both the control and the experimental groups. The superiority margin is set to 0.1.

To complete their sample size study, the researchers want to run an assurance analysis for a range of group sample sizes from 200 to 800. An elicitation exercise determined the prior distributions of the parameters as: $\lambda_1 \sim N(0.7, 0.05)$, $\lambda_2 \sim N(0.45, 0.05)$, $\omega_1 \sim N(0.1, 0.01)$, $\omega_2 \sim N(0.1, 0.01)$, and $A \sim N(50,3)$.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 1** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For	**Assurance**
Prior Entry Method	**Individual (Enter a prior distribution for each applicable parameter)**
Higher Hazard Rates Are	**Worse (H1: λ2 - λ1 < -Δ)**
Alpha	**0.025**
Group Allocation	**Equal (N1 = N2)**
Sample Size Per Group	**200 400 600 800**
Prior Distribution of ω1	**Normal (Mean, SD)**
Mean	**0.1**
SD	**0.01**
Truncation Boundaries	**None**
Prior Distribution of ω2	**Normal (Mean, SD)**
Mean	**0.1**
SD	**0.01**
Truncation Boundaries	**None**
Accrual Time (R)	**1**
Follow-Up Time (T - R)	**2**
Prior Distribution of A	**Normal (Mean, SD)**
Mean	**50**
SD	**3**
Truncation Boundaries	**None**
Prior Distribution of λ1	**Normal (Mean, SD)**
Mean	**0.7**
SD	**0.05**
Truncation Boundaries	**None**

Prior Distribution of λ2....................................**Normal (Mean, SD)**

Mean..**0.45**

SD..**0.05**

Truncation Boundaries...................................**None**

Δ (Superiority Margin)....................................**0.1**

Options Tab
_____

Number of Computation Points for each........**20**
  Prior Distribution

Maximum N1 in Sample Size Search **5000**

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Reports

Numeric Results
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Solve For: Assurance
Groups: 1 = Control, 2 = Treatment
Superiority Margin (Δ): 0.1
Hypotheses: H0: λ2 - λ1 ≥ -Δ vs. H1: λ2 - λ1 < -Δ
Test Statistic: Hazard Rate Difference, λ2 - λ1
Elapsed Times: Accrual = 1, Follow-Up = 2, Total = 3
Prior Type: Independent Univariate Distributions

Prior Distributions
λ1:   Normal (Mean = 0.7, SD = 0.05).
λ2:   Normal (Mean = 0.45, SD = 0.05).
ω1:   Normal (Mean = 0.1, SD = 0.01).
ω2:   Normal (Mean = 0.1, SD = 0.01).
A: Normal (Mean = 50, SD = 3).
_____

		Required Number of Events			Sample Size			Expected Hazard Rate Group 1	Expected Hazard Rate Group 2	Expected Loss Hazard Rate Group 1	Expected Loss Hazard Rate Group 2	Expected Percent Accrual Time until 50% Accrued	
Assurance*	Power‡	E1	E2	E	N1	N2	N	E(λ1)	E(λ2)	E(ω1)	E(ω2)	E(A)	Alpha
0.54992	0.57117	151	122	272	200	200	400	0.7	0.45	0.1	0.1	50	0.025
0.73082	0.85667	301	243	545	400	400	800	0.7	0.45	0.1	0.1	50	0.025
0.80872	0.95954	452	365	817	600	600	1200	0.7	0.45	0.1	0.1	50	0.025
0.85022	0.98979	603	487	1089	800	800	1600	0.7	0.45	0.1	0.1	50	0.025

* The number of points used for computation of the prior(s) was 20.
‡ Power was calculated using λ1 = E(λ1) = 0.7, λ2 = E(λ2) = 0.45, ω1 = E(ω1) = 0.1, ω2 = E(ω2) = 0.1, and A = E(A) = 50.

Assurance	The expected power where the expectation is with respect to the prior distribution(s).
Power	The power calculated using the means of the prior distributions as the values of the corresponding parameters.
E1	The required number of events in group 1.
E2	The required number of events in group 2.
E	The total number of required events . E = E1 + E2.
N1	The number of subjects in group 1.
N2	The number of subjects in group 2.
N	The total sample size. N = N1 + N2.
$E(\lambda 1)$	The expected hazard rate in group 1.
$E(\lambda 2)$	The expected hazard rate in group 2.
$E(\omega 1)$	The expected hazard rate at which subjects in group 1 are lost to follow-up.
$E(\omega 2)$	The expected hazard rate at which subjects in group 2 are lost to follow-up.
E(A)	The expected percent of the accrual time until 50% of the subjects are accrued.
Alpha	The probability of rejecting a true null hypothesis.

Summary Statements
──

A parallel two-group design will be used to test whether the Group 2 (treatment) hazard rate is superior to the Group 1 (control) hazard rate by a margin, with a superiority margin of 0.1 (H0: $\lambda 2 - \lambda 1 \geq -0.1$ versus H1: $\lambda 2 - \lambda 1 <$ -0.1). The comparison will be made using a one-sided, two-sample Z-test of the hazard rate difference, with a Type I error rate (α) of 0.025. It is intended that subjects will enter the study during an accrual period of 1 time unit(s). The follow-up period is 2 time unit(s). It is assumed that the survival times are exponentially distributed. The prior distribution used for the hazard rate in Group 1 is Normal (Mean = 0.7, SD = 0.05). The prior distribution used for the hazard rate in Group 2 is Normal (Mean = 0.45, SD = 0.05). The prior distribution used for the loss hazard rate in Group 1 is Normal (Mean = 0.1, SD = 0.01). The prior distribution used for the loss hazard rate in Group 2 is Normal (Mean = 0.1, SD = 0.01). The prior distribution used for the percent of accrual time until 50% are accrued is Normal (Mean = 50, SD = 3). With sample sizes of 200 for Group 1 (control) and 200 for Group 2 (treatment), the assurance (average power) is 0.54992.
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References
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O'Hagan, A., Stevens, J.W., and Campbell, M.J. 2005. 'Assurance in clinical trial design'. Pharmaceutical Statistics, Volume 4, Pages 187-201.

Ciarleglio, M.M., Arendt, C.D., and Peduzzi, P.N. 2016. 'Selection of the effect size for sample size determination for a continuous response in a superiority clinical trial using a hybrid classical and Bayesian procedure'. Clinical Trials, Volume 13(3), pages 275-285.

Dias, L.C., Morton, A., and Quigley, J. 2018. Elicitation, The Science and Art of Structuring Judgement. Springer.

Chow, S.C., Shao, J., Wang, H., and Lokhnygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida. Section 7.2.1, Page 152.

Lachin, John M. and Foulkes, Mary A. 1986. 'Evaluation of Sample Size and Power for Analyses of Survival with Allowance for Nonuniform Patient Entry, Losses to Follow-up, Noncompliance, and Stratification', Biometrics, Volume 42, September, pages 507-516.
──

These reports show the assurance values obtained by each sample size.

Plots Section

Plots
_____
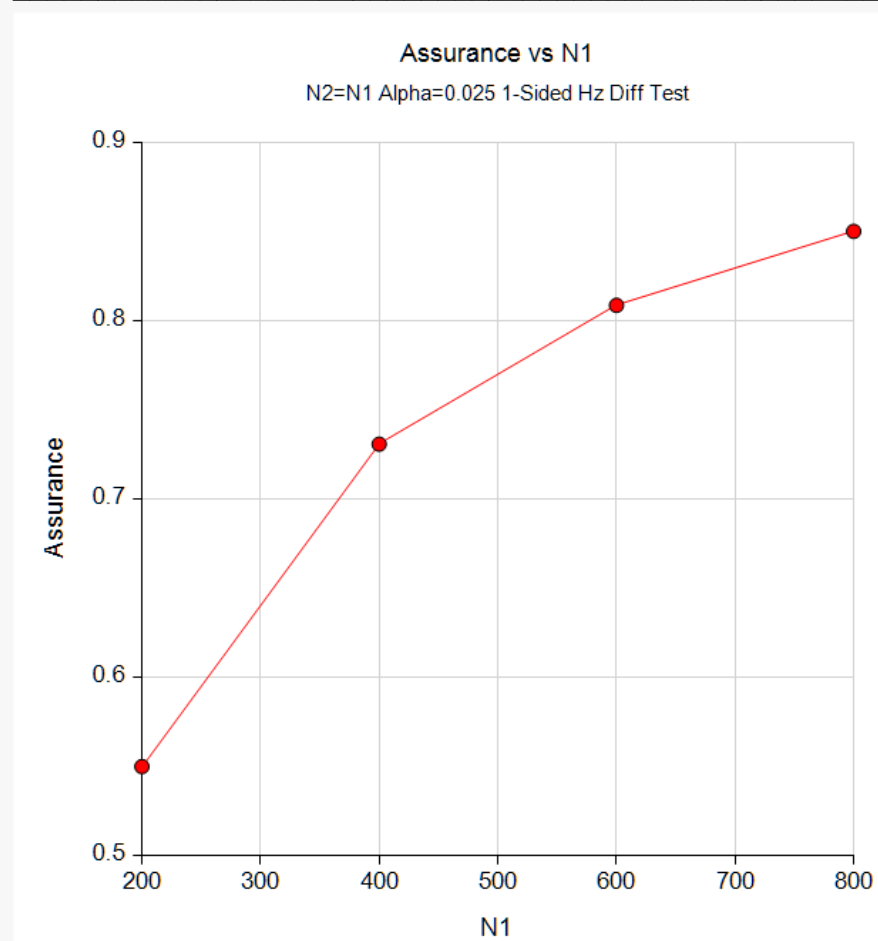
This plot shows the relationship between the assurance and sample size.

Comparison Plots Section

Comparison Plots
_____
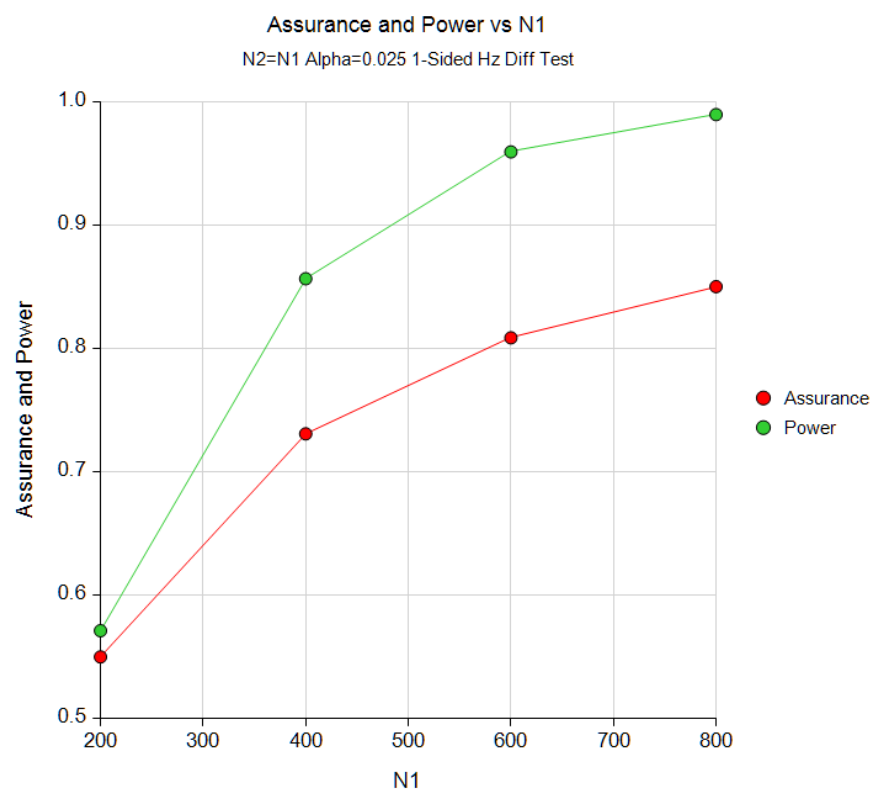
This plot compares the assurance and power across values of sample size.

Example 2 – Validation using Hand Computation

We could not find a validation example in the literature for this procedure, so we have developed a validation example of our own.

Suppose a superiority test of the difference between hazard rates will be used in which the superiority margin is 0.1, N1 = N2 = 200, and the significance level is 0.025.

The prior distribution of $\lambda 1$ is approximated by the following table. These are loaded into C1 and C2.

$\lambda 1$	Prob
0.6	0.4
0.7	0.6

The prior distribution of the $\lambda 2$ is approximated by the following table. These are loaded into C3 and C4.

$\lambda 2$	Prob
0.3	0.4
0.4	0.6

The prior distribution of the $\omega 1$ is approximated by the following table. These are loaded into C5 and C6.

$\omega 1$	Prob
0.10	0.5
0.16	0.5

The prior distribution of the $\omega 2$ is approximated by the following table. These are loaded into C7 and C8.

$\omega 2$	Prob
0.10	0.5
0.16	0.5

The prior distribution of the A is approximated by the following table. These are loaded into C9 and C10.

A	Prob
30	0.5
50	0.5

To run this example, the spreadsheet will need to be loaded with the following ten columns corresponding to the values listed above.

C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
0.6	0.4	0.3	0.4	0.1	0.5	0.1	0.5	30	0.5
0.7	0.6	0.4	0.6	0.16	0.5	0.16	0.5	50	0.5

The *Superiority by a Margin Tests for the Difference of Two Hazard Rates Assuming an Exponential Model* procedure is used to compute the power for each of the 32 parameter combinations. Note that the first report is for *A* = 30 and the next report is for *A* = 50 (Uniform).

Numeric Results

Solve For: Power
Groups: 1 = Control, 2 = Treatment
Hypotheses: H0: h2 ≥ h1 - Δ   vs.   Ha: h2 < h1 - Δ
Accrual: 30% of Accrual Time Results in 50% of Total Enrollment

	Sample Size			Hazard Rate		Hazard Rate Difference	Superiority		Loss Hazard Rate		Time			
Power	N	N1	N2	h1	h2	D	Margin Δ	Boundary B	ω1	ω2	Accrual R	Follow-Up T - R	Alpha	Report Row
0.92765	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.10	0.10	1	2	0.025	1
0.36232	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.10	0.10	1	2	0.025	2
0.99669	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.10	0.10	1	2	0.025	3
0.84150	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.10	0.10	1	2	0.025	4
0.92337	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.10	0.16	1	2	0.025	5
0.35570	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.10	0.16	1	2	0.025	6
0.99633	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.10	0.16	1	2	0.025	7
0.83470	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.10	0.16	1	2	0.025	8
0.91771	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.16	0.10	1	2	0.025	9
0.35162	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.16	0.10	1	2	0.025	10
0.99561	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.16	0.10	1	2	0.025	11
0.82806	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.16	0.10	1	2	0.025	12
0.91328	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.16	0.16	1	2	0.025	13
0.34541	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.16	0.16	1	2	0.025	14
0.99518	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.16	0.16	1	2	0.025	15
0.82128	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.16	0.16	1	2	0.025	16

	Number of Events			Percent Group 1	Hazard Ratio	Variance		Report Row
Power	E	E1	E2	%N1	HR	σ²(h1)	σ²(h2)	
0.92765	241.5	144.0	97.6	50	0.50000	0.50009	0.18448	1
0.36232	260.9	144.0	116.9	50	0.66667	0.50009	0.27369	2
0.99669	250.9	153.4	97.6	50	0.42857	0.63902	0.18448	3
0.84150	270.3	153.4	116.9	50	0.57143	0.63902	0.27369	4
0.92337	235.4	144.0	91.5	50	0.50000	0.50009	0.19682	5
0.35570	253.9	144.0	110.0	50	0.66667	0.50009	0.29103	6
0.99633	244.8	153.4	91.5	50	0.42857	0.63902	0.19682	7
0.83470	263.3	153.4	110.0	50	0.57143	0.63902	0.29103	8
0.91771	233.8	136.2	97.6	50	0.50000	0.52846	0.18448	9
0.35162	253.2	136.2	116.9	50	0.66667	0.52846	0.27369	10
0.99561	243.1	145.5	97.6	50	0.42857	0.67332	0.18448	11
0.82806	262.5	145.5	116.9	50	0.57143	0.67332	0.27369	12
0.91328	227.7	136.2	91.5	50	0.50000	0.52846	0.19682	13
0.34541	246.2	136.2	110.0	50	0.66667	0.52846	0.29103	14
0.99518	237.0	145.5	91.5	50	0.42857	0.67332	0.19682	15
0.82128	255.5	145.5	110.0	50	0.57143	0.67332	0.29103	16

Numeric Results

Solve For: Power
Groups: 1 = Control, 2 = Treatment
Hypotheses: H0: h2 ≥ h1 - Δ vs. Ha: h2 < h1 - Δ
Accrual: Uniform

Power	N	N1	N2	h1	h2	Hazard Rate Difference D	Superiority Margin Δ	Superiority Boundary B	Loss Hazard Rate ω1	Loss Hazard Rate ω2	Accrual R	Follow-Up T - R	Alpha	Report Row
0.92190	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.10	0.10	1	2	0.025	1
0.35536	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.10	0.10	1	2	0.025	2
0.99617	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.10	0.10	1	2	0.025	3
0.83398	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.10	0.10	1	2	0.025	4
0.91758	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.10	0.16	1	2	0.025	5
0.34909	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.10	0.16	1	2	0.025	6
0.99577	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.10	0.16	1	2	0.025	7
0.82729	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.10	0.16	1	2	0.025	8
0.91190	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.16	0.10	1	2	0.025	9
0.34524	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.16	0.10	1	2	0.025	10
0.99501	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.16	0.10	1	2	0.025	11
0.82077	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.16	0.10	1	2	0.025	12
0.90745	400	200	200	0.6	0.3	-0.3	0.1	0.5	0.16	0.16	1	2	0.025	13
0.33934	400	200	200	0.6	0.4	-0.2	0.1	0.5	0.16	0.16	1	2	0.025	14
0.99454	400	200	200	0.7	0.3	-0.4	0.1	0.6	0.16	0.16	1	2	0.025	15
0.81411	400	200	200	0.7	0.4	-0.3	0.1	0.6	0.16	0.16	1	2	0.025	16

Power	Number of Events E	E1	E2	Percent Group 1 %N1	Hazard Ratio HR	Variance $\sigma^2(h1)$	Variance $\sigma^2(h2)$	Report Row
0.92190	235.5	141.0	94.4	50	0.50000	0.51054	0.19058	1
0.35536	254.7	141.0	113.7	50	0.66667	0.51054	0.28149	2
0.99617	245.1	150.7	94.4	50	0.42857	0.65039	0.19058	3
0.83398	264.4	150.7	113.7	50	0.57143	0.65039	0.28149	4
0.91758	229.8	141.0	88.8	50	0.50000	0.51054	0.20277	5
0.34909	248.2	141.0	107.2	50	0.66667	0.51054	0.29860	6
0.99577	239.4	150.7	88.8	50	0.42857	0.65039	0.20277	7
0.82729	257.8	150.7	107.2	50	0.57143	0.65039	0.29860	8
0.91190	228.2	133.7	94.4	50	0.50000	0.53849	0.19058	9
0.34524	247.4	133.7	113.7	50	0.66667	0.53849	0.28149	10
0.99501	237.7	143.2	94.4	50	0.42857	0.68417	0.19058	11
0.82077	256.9	143.2	113.7	50	0.57143	0.68417	0.28149	12
0.90745	222.5	133.7	88.8	50	0.50000	0.53849	0.20277	13
0.33934	240.9	133.7	107.2	50	0.66667	0.53849	0.29860	14
0.99454	232.0	143.2	88.8	50	0.42857	0.68417	0.20277	15
0.81411	250.4	143.2	107.2	50	0.57143	0.68417	0.29860	16

The assurance calculation is made by summing the quantities

$$\left[(power_{i,j,k,l,m})p(\lambda 1_i)p(\lambda 2_j)p(\omega 1_k)p(\omega 2_l)p(A_m)\right]$$

as follows

$$Assurance = (0.92765 \times 0.4 \times 0.4 \times 0.5 \times 0.5 \times 0.5) + (0.36232 \times 0.4 \times 0.6 \times 0.5 \times 0.5 \times 0.5) + \cdots$$
$$+ (0.81411 \times 0.6 \times 0.6 \times 0.5 \times 0.5 \times 0.5)$$
$$= 0.76787$$

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 2** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For ....**Assurance**
Prior Entry Method..**Individual (Enter a prior distribution for each applicable parameter)**
Higher Hazard Rates Are...............................**Worse (H1: λ2 - λ1 < -Δ)**
Alpha...**0.025**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group **200**
Prior Distribution of ω1.................................**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C5**
Column of Pr(Values).....................................**C6**
Prior Distribution of ω2.................................**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C7**
Column of Pr(Values).....................................**C8**
Accrual Time (R)..**1**
Follow-Up Time (T - R) **2**
Prior Distribution of A....................................**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C9**
Column of Pr(Values).....................................**C10**
Prior Distribution of λ1..................................**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C1**
Column of Pr(Values).....................................**C2**
Prior Distribution of λ2..................................**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C3**
Column of Pr(Values).....................................**C4**
Δ (Superiority Margin) **0.1**

Options Tab

Number of Computation Points for each........**20**
  Prior Distribution
Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
1	0.6	0.4	0.3	0.4	0.10	0.5	0.10	0.5	50	0.5
2	0.7	0.6	0.4	0.6	0.16	0.5	0.16	0.5	30	0.5

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results

Numeric Results
_____

Solve For:	Assurance
Groups:	1 = Control, 2 = Treatment
Superiority Margin (Δ):	0.1
Hypotheses:	H0: $\lambda 2 - \lambda 1 \geq -\Delta$ vs. H1: $\lambda 2 - \lambda 1 < -\Delta$
Test Statistic:	Hazard Rate Difference, $\lambda 2 - \lambda 1$
Elapsed Times:	Accrual = 1, Follow-Up = 2, Total = 3
Prior Type:	Independent Univariate Distributions

Prior Distributions

$\lambda 1$:   Point List (Values = C1, Probs = C2).
  C1:   0.6 0.7
  C2:   0.4 0.6
$\lambda 2$:   Point List (Values = C3, Probs = C4).
  C3:   0.3 0.4
  C4:   0.4 0.6
$\omega 1$:   Point List (Values = C5, Probs = C6).
  C5:   0.1 0.16
  C6:   0.5 0.5
$\omega 2$:   Point List (Values = C7, Probs = C8).
  C7:   0.1 0.16
  C8:   0.5 0.5
A: Point List (Values = C9, Probs = C10).
  C9:   50 30
  C10: 0.5 0.5
_____

		Required Number of Events			Sample Size			Expected Hazard Rate Group 1	Expected Hazard Rate Group 2	Expected Loss Hazard Rate Group 1	Expected Loss Hazard Rate Group 2	Expected Percent Accrual Time until 50% Accrued	
Assurance	Power‡	E1	E2	E	N1	N2	N	E(λ1)	E(λ2)	E(ω1)	E(ω2)	E(A)	Alpha
0.76787	0.866	145	105	249	200	200	400	0.66	0.36	0.13	0.13	40	0.025

‡ Power was calculated using $\lambda 1 = E(\lambda 1) = 0.66$, $\lambda 2 = E(\lambda 2) = 0.36$, $\omega 1 = E(\omega 1) = 0.13$, $\omega 2 = E(\omega 2) = 0.13$, and $A = E(A) = 40$.

PASS has also calculated the assurance as 0.76787 which validates the procedure.

Example 3 – Finding the Sample Size Needed to Achieve a Specified Assurance

Continuing with Example 1, the researchers want to investigate the sample sizes necessary to achieve assurances of 0.4, 0.5, and 0.6.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 3** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For	**Sample Size**
Prior Entry Method	**Individual (Enter a prior distribution for each applicable parameter)**
Higher Hazard Rates Are	**Worse (H1: λ2 - λ1 < -∆)**
Assurance	**0.4 0.5 0.6**
Alpha	**0.025**
Group Allocation	**Equal (N1 = N2)**
Prior Distribution of ω1	**Normal (Mean, SD)**
Mean	**0.1**
SD	**0.01**
Truncation Boundaries	**None**
Prior Distribution of ω2	**Normal (Mean, SD)**
Mean	**0.1**
SD	**0.01**
Truncation Boundaries	**None**
Accrual Time (R)	**1**
Follow-Up Time (T - R)	**2**
Prior Distribution of A	**Normal (Mean, SD)**
Mean	**50**
SD	**3**
Truncation Boundaries	**None**
Prior Distribution of λ1	**Normal (Mean, SD)**
Mean	**0.7**
SD	**0.05**
Truncation Boundaries	**None**
Prior Distribution of λ2	**Normal (Mean, SD)**
Mean	**0.45**
SD	**0.05**
Truncation Boundaries	**None**
∆ (Superiority Margin)	**0.2**

Options Tab

Number of Computation Points for each........**10**
 Prior Distribution
Maximum N1 in Sample Size Search **5000**

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Reports

Numeric Results

Solve For: Sample Size
Groups: 1 = Control, 2 = Treatment
Superiority Margin (Δ):   0.2
Hypotheses: H0: λ2 - λ1 ≥ -Δ vs. H1: λ2 - λ1 < -Δ
Test Statistic: Hazard Rate Difference, λ2 - λ1
Elapsed Times: Accrual = 1, Follow-Up = 2, Total = 3
Prior Type: Independent Univariate Distributions

Prior Distributions
λ1: Normal (Mean = 0.7, SD = 0.05).
λ2: Normal (Mean = 0.45, SD = 0.05).
ω1: Normal (Mean = 0.1, SD = 0.01).
ω2: Normal (Mean = 0.1, SD = 0.01).
A: Normal (Mean = 50, SD = 3).

		Required Number of Events			Sample Size			Expected Hazard Rate Group 1	Expected Hazard Rate Group 2	Expected Loss Hazard Rate Group 1	Expected Loss Hazard Rate Group 2	Expected Percent Accrual Time until 50% Accrued	
Assurance*	Power‡	E1	E2	E	N1	N2	N	E(λ1)	E(λ2)	E(ω1)	E(ω2)	E(A)	Alpha
0.40016	0.28903	584	472	1055	775	775	1550	0.7	0.45	0.1	0.1	50	0.025
0.50009	0.50107	1141	922	2063	1515	1515	3030	0.7	0.45	0.1	0.1	50	0.025
0.60002	0.87230	2842	2296	5138	3773	3773	7546	0.7	0.45	0.1	0.1	50	0.025

* The number of points used for computation of the prior(s) was 10.
‡ Power was calculated using λ1 = E(λ1) = 0.7, λ2 = E(λ2) = 0.45, ω1 = E(ω1) = 0.1, ω2 = E(ω2) = 0.1, and A = E(A) = 50.

Plots Section

Plots
_____
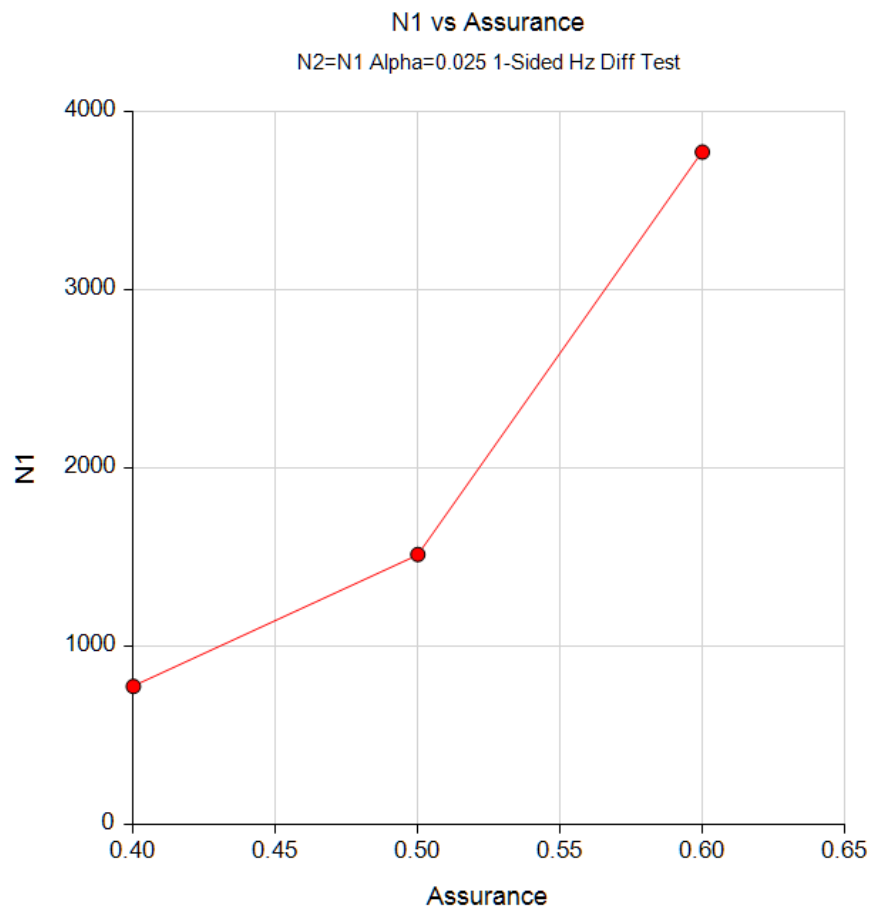
This plot shows the relationship between the assurance and sample size.

Example 4 – Joint Prior Distribution

The following example shows the complexity required to specify a joint distribution for five parameters.

Suppose a superiority by a margin test will be used in which N1 = N2 = (200 400 600 800) and the significance level is 0.025. The superiority margin is set at 0.1. Further suppose that the joint prior distribution of the parameters is approximated by the following table. In a real study, the values in this table would be provided by an elicitation study.

Note that the program will rescale the probabilities so they sum to one.

λ1	λ2	ω1	ω2	A	Prob
0.6	0.3	0.05	0.05	30	0.07
0.6	0.3	0.1	0.1	30	0.09
0.6	0.3	0.15	0.15	30	0.11
0.65	0.3	0.05	0.05	30	0.07
0.65	0.3	0.1	0.1	30	0.09
0.65	0.3	0.15	0.15	30	0.11
0.7	0.3	0.05	0.05	30	0.07
0.7	0.3	0.1	0.1	30	0.09
0.7	0.3	0.15	0.15	30	0.11
0.6	0.4	0.05	0.05	30	0.27
0.6	0.4	0.1	0.1	30	0.29
0.6	0.4	0.15	0.15	30	0.31
0.65	0.4	0.05	0.05	30	0.27
0.65	0.4	0.1	0.1	30	0.29
0.65	0.4	0.15	0.15	30	0.31
0.7	0.4	0.05	0.05	30	0.27
0.7	0.4	0.1	0.1	30	0.29
0.7	0.4	0.15	0.15	30	0.31
0.6	0.5	0.05	0.05	30	0.17
0.6	0.5	0.1	0.1	30	0.19
0.6	0.5	0.15	0.15	30	0.21
0.65	0.5	0.05	0.05	30	0.17
0.65	0.5	0.1	0.1	30	0.19
0.65	0.5	0.15	0.15	30	0.21
0.7	0.5	0.05	0.05	30	0.17
0.7	0.5	0.1	0.1	30	0.19
0.7	0.5	0.15	0.15	30	0.21
0.6	0.3	0.05	0.05	50	0.12
0.6	0.3	0.1	0.1	50	0.14
0.6	0.3	0.15	0.15	50	0.16
0.65	0.3	0.05	0.05	50	0.12
0.65	0.3	0.1	0.1	50	0.14
0.65	0.3	0.15	0.15	50	0.16
0.7	0.3	0.05	0.05	50	0.12
0.7	0.3	0.1	0.1	50	0.14
0.7	0.3	0.15	0.15	50	0.16

Assurance for Superiority by a Margin Tests for the Difference of Two Hazard Rates Assuming an Exponential Model

0.6	0.4	0.05	0.05	50	0.32
0.6	0.4	0.1	0.1	50	0.34
0.6	0.4	0.15	0.15	50	0.36
0.65	0.4	0.05	0.05	50	0.32
0.65	0.4	0.1	0.1	50	0.34
0.65	0.4	0.15	0.15	50	0.36
0.7	0.4	0.05	0.05	50	0.32
0.7	0.4	0.1	0.1	50	0.34
0.7	0.4	0.15	0.15	50	0.36
0.6	0.5	0.05	0.05	50	0.22
0.6	0.5	0.1	0.1	50	0.24
0.6	0.5	0.15	0.15	50	0.26
0.65	0.5	0.05	0.05	50	0.22
0.65	0.5	0.1	0.1	50	0.24
0.65	0.5	0.15	0.15	50	0.26
0.7	0.5	0.05	0.05	50	0.22
0.7	0.5	0.1	0.1	50	0.24
0.7	0.5	0.15	0.15	50	0.26
0.6	0.3	0.05	0.05	70	0.07
0.6	0.3	0.1	0.1	70	0.09
0.6	0.3	0.15	0.15	70	0.11
0.65	0.3	0.05	0.05	70	0.07
0.65	0.3	0.1	0.1	70	0.09
0.65	0.3	0.15	0.15	70	0.11
0.7	0.3	0.05	0.05	70	0.07
0.7	0.3	0.1	0.1	70	0.09
0.7	0.3	0.15	0.15	70	0.11
0.6	0.4	0.05	0.05	70	0.27
0.6	0.4	0.1	0.1	70	0.29
0.6	0.4	0.15	0.15	70	0.31
0.65	0.4	0.05	0.05	70	0.27
0.65	0.4	0.1	0.1	70	0.29
0.65	0.4	0.15	0.15	70	0.31
0.7	0.4	0.05	0.05	70	0.27
0.7	0.4	0.1	0.1	70	0.29
0.7	0.4	0.15	0.15	70	0.31
0.6	0.5	0.05	0.05	70	0.17
0.6	0.5	0.1	0.1	70	0.19
0.6	0.5	0.15	0.15	70	0.21
0.65	0.5	0.05	0.05	70	0.17
0.65	0.5	0.1	0.1	70	0.19
0.65	0.5	0.15	0.15	70	0.21
0.7	0.5	0.05	0.05	70	0.17
0.7	0.5	0.1	0.1	70	0.19
0.7	0.5	0.15	0.15	70	0.21

To run this example, the above data will need to be loaded into columns C1 to C6.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 4** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For ....**Assurance**
Prior Entry Method..**Combined (Enter parameter values and probabilities on spreadsheet)**
Higher Hazard Rates Are...............................**Worse (H1: λ2 - λ1 < -∆)**
Alpha..**0.025**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group **200 400 600 800**
Column of ω1 Values.....................................**C3**
Column of ω2 Values.....................................**C4**
Accrual Time (R)...**1**
Follow-Up Time (T - R) **2**
Column of A Values **C5**
Column of λ1 Values......................................**C1**
Column of λ2 Values......................................**C2**
Column of Pr(Values).....................................**C6**
∆ (Superiority Margin) **0.1**

Options Tab

Number of Computation Points for each........**10**
  Prior Distribution
Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6
1	0.60	0.3	0.05	0.05	30	0.07
2	0.60	0.3	0.10	0.10	30	0.09
3	0.60	0.3	0.15	0.15	30	0.11
4	0.65	0.3	0.05	0.05	30	0.07
5	0.65	0.3	0.10	0.10	30	0.09
6	0.65	0.3	0.15	0.15	30	0.11
7	0.70	0.3	0.05	0.05	30	0.07
8	0.70	0.3	0.10	0.10	30	0.09
9	0.70	0.3	0.15	0.15	30	0.11
10	0.60	0.4	0.05	0.05	30	0.27
11	0.60	0.4	0.10	0.10	30	0.29
12	0.60	0.4	0.15	0.15	30	0.31
13	0.65	0.4	0.05	0.05	30	0.27
14	0.65	0.4	0.10	0.10	30	0.29
15	0.65	0.4	0.15	0.15	30	0.31
16	0.70	0.4	0.05	0.05	30	0.27
17	0.70	0.4	0.10	0.10	30	0.29
18	0.70	0.4	0.15	0.15	30	0.31
19	0.60	0.5	0.05	0.05	30	0.17
20	0.60	0.5	0.10	0.10	30	0.19
21	0.60	0.5	0.15	0.15	30	0.21

Assurance for Superiority by a Margin Tests for the Difference of Two Hazard Rates Assuming an Exponential Model

22	0.65	0.5	0.05	0.05	30	0.17
23	0.65	0.5	0.10	0.10	30	0.19
24	0.65	0.5	0.15	0.15	30	0.21
25	0.70	0.5	0.05	0.05	30	0.17
26	0.70	0.5	0.10	0.10	30	0.19
27	0.70	0.5	0.15	0.15	30	0.21
28	0.60	0.3	0.05	0.05	50	0.12
29	0.60	0.3	0.10	0.10	50	0.14
30	0.60	0.3	0.15	0.15	50	0.16
31	0.65	0.3	0.05	0.05	50	0.12
32	0.65	0.3	0.10	0.10	50	0.14
33	0.65	0.3	0.15	0.15	50	0.16
34	0.70	0.3	0.05	0.05	50	0.12
35	0.70	0.3	0.10	0.10	50	0.14
36	0.70	0.3	0.15	0.15	50	0.16
37	0.60	0.4	0.05	0.05	50	0.32
38	0.60	0.4	0.10	0.10	50	0.34
39	0.60	0.4	0.15	0.15	50	0.36
40	0.65	0.4	0.05	0.05	50	0.32
41	0.65	0.4	0.10	0.10	50	0.34
42	0.65	0.4	0.15	0.15	50	0.36
43	0.70	0.4	0.05	0.05	50	0.32
44	0.70	0.4	0.10	0.10	50	0.34
45	0.70	0.4	0.15	0.15	50	0.36
46	0.60	0.5	0.05	0.05	50	0.22
47	0.60	0.5	0.10	0.10	50	0.24
48	0.60	0.5	0.15	0.15	50	0.26
49	0.65	0.5	0.05	0.05	50	0.22
50	0.65	0.5	0.10	0.10	50	0.24
51	0.65	0.5	0.15	0.15	50	0.26
52	0.70	0.5	0.05	0.05	50	0.22
53	0.70	0.5	0.10	0.10	50	0.24
54	0.70	0.5	0.15	0.15	50	0.26
55	0.60	0.3	0.05	0.05	70	0.07
56	0.60	0.3	0.10	0.10	70	0.09
57	0.60	0.3	0.15	0.15	70	0.11
58	0.65	0.3	0.05	0.05	70	0.07
59	0.65	0.3	0.10	0.10	70	0.09
60	0.65	0.3	0.15	0.15	70	0.11
61	0.70	0.3	0.05	0.05	70	0.07
62	0.70	0.3	0.10	0.10	70	0.09
63	0.70	0.3	0.15	0.15	70	0.11
64	0.60	0.4	0.05	0.05	70	0.27
65	0.60	0.4	0.10	0.10	70	0.29
66	0.60	0.4	0.15	0.15	70	0.31
67	0.65	0.4	0.05	0.05	70	0.27
68	0.65	0.4	0.10	0.10	70	0.29
69	0.65	0.4	0.15	0.15	70	0.31
70	0.70	0.4	0.05	0.05	70	0.27
71	0.70	0.4	0.10	0.10	70	0.29
72	0.70	0.4	0.15	0.15	70	0.31
73	0.60	0.5	0.05	0.05	70	0.17
74	0.60	0.5	0.10	0.10	70	0.19
75	0.60	0.5	0.15	0.15	70	0.21
76	0.65	0.5	0.05	0.05	70	0.17
77	0.65	0.5	0.10	0.10	70	0.19
78	0.65	0.5	0.15	0.15	70	0.21
79	0.70	0.5	0.05	0.05	70	0.17
80	0.70	0.5	0.10	0.10	70	0.19
81	0.70	0.5	0.15	0.15	70	0.21

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results
───

Solve For:	Assurance
Groups:	1 = Control, 2 = Treatment
Superiority Margin (Δ):	0.1
Hypotheses:	H0: $\lambda 2 - \lambda 1 \geq -\Delta$ vs. H1: $\lambda 2 - \lambda 1 < -\Delta$
Test Statistic:	Hazard Rate Difference, $\lambda 2 - \lambda 1$
Elapsed Times:	Accrual = 1, Follow-Up = 2, Total = 3
Prior Type:	Joint Multivariate Distribution

Prior Distribution
Point Lists
$\lambda 1$: C1: 0.6 0.6 0.6 0.65 0.65 0.65 0.7 0.7 0.7 0.6 0.6 0.6 0.65 0.65 0.65 0.7 0.7 0.7 0.6 0.6 0.6 0.65 0.65 0.65 0.7 0.7 0.7 0.6 0.6 0.6 0.65
         0.65 0.65 0.7 0.7 0.7 0.6 0.6 0.6 0.65 0.65 0.65 0.7 0.7 0.7 0.6 0.6 0.6 0.65 0.65 0.65 0.7 0.7 0.7 0.6 0.6 0.6 0.65 0.65 0.65 0.7
         0.7 0.7 0.6 0.6 0.6 0.65 0.65 0.65 0.7 0.7 0.7 0.6 0.6 0.6 0.65 0.65 0.65 0.7 0.7 0.7

$\lambda 2$: C2: 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.3 0.3 0.3 0.3 0.3 0.3 0.3
         0.3 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.4 0.4 0.4 0.4 0.4
         0.4 0.4 0.4 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5

$\omega 1$: C3: 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05
         0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1
         0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15

$\omega 2$: C4: 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05
         0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1
         0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15 0.05 0.1 0.15

A: C5: 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 50 50 50 50 50 50 50 50 50
         50 50 50 50 50 50 50 50 50 50 50 50 50 50 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70 70

Prob: C6: 0.07 0.09 0.11 0.07 0.09 0.11 0.07 0.09 0.11 0.27 0.29 0.31 0.27 0.29 0.31 0.27 0.29 0.31 0.17 0.19 0.21 0.17 0.19 0.21 0.17 0.19
         0.21 0.12 0.14 0.16 0.12 0.14 0.16 0.12 0.14 0.16 0.32 0.34 0.36 0.32 0.34 0.36 0.32 0.34 0.36 0.22 0.24 0.26 0.22 0.24 0.26
         0.22 0.24 0.26 0.07 0.09 0.11 0.07 0.09 0.11 0.07 0.09 0.11 0.27 0.29 0.31 0.27 0.29 0.31 0.27 0.29 0.31 0.17 0.19 0.21 0.17
         0.19 0.21 0.17 0.19 0.21
───

		Required Number of Events			**Sample Size**			**Expected Hazard Rate Group 1**	**Expected Hazard Rate Group 2**	**Expected Loss Hazard Rate Group 1**	**Expected Loss Hazard Rate Group 2**	**Expected Percent of Accrual Time until 50% are Accrued**	
Assurance	**Power‡**	**E1**	**E2**	**E**	**N1**	**N2**	**N**	**E($\lambda 1$)**	**E($\lambda 2$)**	**E($\omega 1$)**	**E($\omega 2$)**	**E(A)**	**Alpha**
0.51157	0.52384	146	116	262	200	200	400	0.65	0.41613	0.10323	0.10323	50	0.025
0.66083	0.81498	291	232	523	400	400	800	0.65	0.41613	0.10323	0.10323	50	0.025
0.73082	0.93802	437	348	785	600	600	1200	0.65	0.41613	0.10323	0.10323	50	0.025
0.77143	0.98122	583	464	1047	800	800	1600	0.65	0.41613	0.10323	0.10323	50	0.025

‡ Power was calculated using $\lambda 1 = E(\lambda 1) = 0.65$, $\lambda 2 = E(\lambda 2) = 0.41613$, $\omega 1 = E(\omega 1) = 0.10323$, $\omega 2 = E(\omega 2) = 0.10323$, and A = E(A) = 50.

This report shows the assurance values obtained by each sample size.

Example 5 – Joint Prior Validation

The problem given in Example 2 will be used to validate the joint prior distribution method. This will be done by running the independent-prior scenario used in that example through the joint-prior method and checking that the assurance values match.

In Example 2, the prior distributions of the parameters are

λ1	P(λ1)	λ2	P(λ2)	ω1	P(ω1)	ω2	P(ω2)	A	P(A)
0.6	0.4	0.3	0.4	0.1	0.5	0.1	0.5	30	0.5
0.7	0.6	0.4	0.6	0.16	0.5	0.16	0.5	50	0.5

The joint prior distribution can be found by multiplying the five independent probabilities in each row. This results in the following discrete joint probability distribution.

λ1	λ2	ω1	ω2	A	Prob
0.6	0.3	0.1	0.1	30	0.02
0.6	0.4	0.1	0.1	30	0.03
0.7	0.3	0.1	0.1	30	0.03
0.7	0.4	0.1	0.1	30	0.045
0.6	0.3	0.1	0.16	30	0.02
0.6	0.4	0.1	0.16	30	0.03
0.7	0.3	0.1	0.16	30	0.03
0.7	0.4	0.1	0.16	30	0.045
0.6	0.3	0.16	0.1	30	0.02
0.6	0.4	0.16	0.1	30	0.03
0.7	0.3	0.16	0.1	30	0.03
0.7	0.4	0.16	0.1	30	0.045
0.6	0.3	0.16	0.16	30	0.02
0.6	0.4	0.16	0.16	30	0.03
0.7	0.3	0.16	0.16	30	0.03
0.7	0.4	0.16	0.16	30	0.045
0.6	0.3	0.1	0.1	50	0.02
0.6	0.4	0.1	0.1	50	0.03
0.7	0.3	0.1	0.1	50	0.03
0.7	0.4	0.1	0.1	50	0.045
0.6	0.3	0.1	0.16	50	0.02
0.6	0.4	0.1	0.16	50	0.03
0.7	0.3	0.1	0.16	50	0.03
0.7	0.4	0.1	0.16	50	0.045
0.6	0.3	0.16	0.1	50	0.02
0.6	0.4	0.16	0.1	50	0.03
0.7	0.3	0.16	0.1	50	0.03
0.7	0.4	0.16	0.1	50	0.045
0.6	0.3	0.16	0.16	50	0.02
0.6	0.4	0.16	0.16	50	0.03
0.7	0.3	0.16	0.16	50	0.03
0.7	0.4	0.16	0.16	50	0.045

To run this example, the spreadsheet is loaded with the following six columns.

C1	C2	C3	C4	C5	C6
0.6	0.3	0.1	0.1	30	0.02
0.6	0.4	0.1	0.1	30	0.03
0.7	0.3	0.1	0.1	30	0.03
0.7	0.4	0.1	0.1	30	0.045
0.6	0.3	0.1	0.16	30	0.02
0.6	0.4	0.1	0.16	30	0.03
0.7	0.3	0.1	0.16	30	0.03
0.7	0.4	0.1	0.16	30	0.045
0.6	0.3	0.16	0.1	30	0.02
0.6	0.4	0.16	0.1	30	0.03
0.7	0.3	0.16	0.1	30	0.03
0.7	0.4	0.16	0.1	30	0.045
0.6	0.3	0.16	0.16	30	0.02
0.6	0.4	0.16	0.16	30	0.03
0.7	0.3	0.16	0.16	30	0.03
0.7	0.4	0.16	0.16	30	0.045
0.6	0.3	0.1	0.1	50	0.02
0.6	0.4	0.1	0.1	50	0.03
0.7	0.3	0.1	0.1	50	0.03
0.7	0.4	0.1	0.1	50	0.045
0.6	0.3	0.1	0.16	50	0.02
0.6	0.4	0.1	0.16	50	0.03
0.7	0.3	0.1	0.16	50	0.03
0.7	0.4	0.1	0.16	50	0.045
0.6	0.3	0.16	0.1	50	0.02
0.6	0.4	0.16	0.1	50	0.03
0.7	0.3	0.16	0.1	50	0.03
0.7	0.4	0.16	0.1	50	0.045
0.6	0.3	0.16	0.16	50	0.02
0.6	0.4	0.16	0.16	50	0.03
0.7	0.3	0.16	0.16	50	0.03
0.7	0.4	0.16	0.16	50	0.045

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 5** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For ....**Assurance**
Prior Entry Method.......................................**Combined (Enter parameter values and**
                             probabilities on spreadsheet)
Higher Hazard Rates Are...............................**Worse (H1: λ2 - λ1 < -∆)**
Alpha...**0.025**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group **200**
Column of ω1 Values....................................**C3**
Column of ω2 Values....................................**C4**
Accrual Time (R)...**1**
Follow-Up Time (T - R) **2**
Column of A Values **C5**
Column of λ1 Values.....................................**C1**
Column of λ2 Values.....................................**C2**
Column of Pr(Values).....................................**C6**
∆ (Superiority Margin) **0.1**

Options Tab

Number of Computation Points for each........**10**
  Prior Distribution
Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6
1	0.6	0.3	0.10	0.10	30	0.020
2	0.6	0.4	0.10	0.10	30	0.030
3	0.7	0.3	0.10	0.10	30	0.030
4	0.7	0.4	0.10	0.10	30	0.045
5	0.6	0.3	0.10	0.16	30	0.020
6	0.6	0.4	0.10	0.16	30	0.030
7	0.7	0.3	0.10	0.16	30	0.030
8	0.7	0.4	0.10	0.16	30	0.045
9	0.6	0.3	0.16	0.10	30	0.020
10	0.6	0.4	0.16	0.10	30	0.030
11	0.7	0.3	0.16	0.10	30	0.030
12	0.7	0.4	0.16	0.10	30	0.045
13	0.6	0.3	0.16	0.16	30	0.020
14	0.6	0.4	0.16	0.16	30	0.030
15	0.7	0.3	0.16	0.16	30	0.030
16	0.7	0.4	0.16	0.16	30	0.045
17	0.6	0.3	0.10	0.10	50	0.020
18	0.6	0.4	0.10	0.10	50	0.030
19	0.7	0.3	0.10	0.10	50	0.030
20	0.7	0.4	0.10	0.10	50	0.045
21	0.6	0.3	0.10	0.16	50	0.020

22	0.6	0.4	0.10	0.16	50	0.030
23	0.7	0.3	0.10	0.16	50	0.030
24	0.7	0.4	0.10	0.16	50	0.045
25	0.6	0.3	0.16	0.10	50	0.020
26	0.6	0.4	0.16	0.10	50	0.030
27	0.7	0.3	0.16	0.10	50	0.030
28	0.7	0.4	0.16	0.10	50	0.045
29	0.6	0.3	0.16	0.16	50	0.020
30	0.6	0.4	0.16	0.16	50	0.030
31	0.7	0.3	0.16	0.16	50	0.030
32	0.7	0.4	0.16	0.16	50	0.045

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results

Solve For:	Assurance
Groups:	1 = Control, 2 = Treatment
Superiority Margin (Δ):	0.1
Hypotheses:	H0: $\lambda 2 - \lambda 1 \geq -\Delta$ vs. H1: $\lambda 2 - \lambda 1 < -\Delta$
Test Statistic:	Hazard Rate Difference, $\lambda 2 - \lambda 1$
Elapsed Times:	Accrual = 1, Follow-Up = 2, Total = 3
Prior Type:	Joint Multivariate Distribution

Prior Distribution

Point Lists

$\lambda 1$:　C1:　0.6 0.6 0.7 0.7 0.6 0.6 0.7 0.7 0.6 0.6 0.7 0.7 0.6 0.6 0.7 0.7 0.6 0.6 0.7 0.7 0.6 0.6 0.7 0.7 0.6 0.6 0.7 0.7 0.6 0.6 0.7 0.7

$\lambda 2$:　C2:　0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4 0.3 0.4

$\omega 1$:　C3:　0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.16 0.16 0.16 0.16 0.16 0.16 0.16 0.16 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.16 0.16 0.16 0.16 0.16 0.16 0.16 0.16

$\omega 2$:　C4:　0.1 0.1 0.1 0.1 0.16 0.16 0.16 0.16 0.1 0.1 0.1 0.1 0.16 0.16 0.16 0.16 0.1 0.1 0.1 0.1 0.16 0.16 0.16 0.16 0.1 0.1 0.1 0.1 0.16 0.16 0.16 0.16

A:　C5:　30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 30 50 50 50 50 50 50 50 50 50 50 50 50 50 50 50 50

Prob:　C6:　0.02 0.03 0.03 0.045 0.02 0.03 0.03 0.045 0.02 0.03 0.03 0.045 0.02 0.03 0.03 0.045 0.02 0.03 0.03 0.045 0.02 0.03 0.03 0.045 0.02 0.03 0.03 0.045 0.02 0.03 0.03 0.045

		Required Number of Events			Sample Size			Expected Hazard Rate Group 1	Expected Hazard Rate Group 2	Expected Loss Hazard Rate Group 1	Expected Loss Hazard Rate Group 2	Expected Percent of Accrual Time until 50% are Accrued	
Assurance	Power‡	E1	E2	E	N1	N2	N	E($\lambda 1$)	E($\lambda 2$)	E($\omega 1$)	E($\omega 2$)	E(A)	Alpha
0.76787	0.866	145	105	249	200	200	400	0.66	0.36	0.13	0.13	40	0.025

‡ Power was calculated using $\lambda 1 = E(\lambda 1) = 0.66$, $\lambda 2 = E(\lambda 2) = 0.36$, $\omega 1 = E(\omega 1) = 0.13$, $\omega 2 = E(\omega 2) = 0.13$, and A = E(A) = 40.

PASS has also calculated the assurance as 0.76787 which matches Example 2 and thus validates the procedure.